SHORT PAPER

A mild and efficient method for the mononitration of aromatic compounds by cerium (III) ammonium nitrate in acetic anhydride[†]

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A mild and efficient method for the mononitration of aromatic and olefinic compounds is described. This method is especially useful for active substrates.

Keywords: mononitration, aromatic compounds, acetic anhydride, cerium (III) ammonium nitrate

Nitration of aromatic compounds is a transformation of considerable importance in synthetic organic chemistry.[1] For this purpose, a mixture of HNO_3 and H_2SO_4 is the most common reagent. The reagent system HNO_3–acetic anhydride (Ac_2O) is frequently used for acid-sensitive or active substrates. In this case, cooling to a low temperature is necessary because of the intense exothermic reactions.[2] The reagent system $Cu(NO_3)_2$–Ac_2O is also known. However, it is difficult to control the reaction temperature.[3] Due to the reasons mentioned above, nitration often resulted in a complex mixture involving large amounts of decomposed materials. Recently, cerium (IV) ammonium nitrate (CAN)-mediated nitration of aromatic and other systems have been reported.[4,5]

In the course of our continuing studies on deprotection, we observed the generation of acetyl nitrate by the reaction of CAN with Ac_2O.[6] In this context, we supposed the use of acetyl nitrate produced by the reaction of cerium(III) ammonium nitrate (**13**) with Ac_2O for aromatic nitration. We chose the Ce(III) salt in order to avoid oxidative side reactions caused by the Ce(IV) salt. In this paper, we report that aromatic and olefinic compounds are nitrated with **13** in Ac_2O under mild conditions.

First, the nitration of 1,4-dimethoxybenzene (**1a**) was chosen as a model reaction. Compound **13** (1.0 mmol) was treated with **1a** (5.0 mmol) in Ac_2O at room temperature for 14 h to afford 1,4-dimethoxy-2-nitrobenzene (2.68 mmol) together with the recovery of **1a** (1.88 mmol). This experiment suggests that **13** was found to react with 3 equiv. of substrates.

The reactions of various compounds with **13** in Ac_2O were examined. The results are summarised in Table 1. The reactions of aromatic compounds **1a–3a** led to the corresponding nitro compounds in good yields (entries 1–3). The ratio of *o*-, *m*- and *p*-nitrotoluene (54, 4 and 34%) is almost same as that using HNO_3–H_2SO_4 (56, 5 and 38%) (entry 2).[7] The yield (82%) of **3b** for the present reaction is higher than that (67%) using $Cu(NO_3)_2$ in Ac_2O.[3] The nitration of compounds possessing electron-withdrawing groups such as acetophenone and methyl benzoate did not proceed at 60 °C. Electron-rich heterocyclic compounds **4a–9a** reacted with **13** in Ac_2O at room temperature to afford nitro compounds (entries 4–9). It is noteworthy to point out that cooling is not necessary for most of substrates examined. Only the reaction of pyrrole (**5a**) required cooling with a water bath to prevent the heating of the reaction mixture above room

temperature. When the nitration of pyrrole (**5a**) is performed with HNO_3 in Ac_2O, the reaction must be carried out at –20 °C with precise temperature control.[8]

We compared the present method with the others for the nitration of furan (**6a**). It has been reported that furan (**6a**) reacted with HNO_3 in Ac_2O at –5 °C to give the adduct **6b** in 69% yield, which was converted into 2-nitrofuran by treatment with pyridine.[9] The present procedure using **13** in Ac_2O proceeded at room temperature to give the adduct **6b** in 67% yield. When furan (**6a**) was nitrated with $Cu(NO_3)_2$ in Ac_2O at room temperature, only a small amount of **6b** (2%) was obtained together with large amounts of decomposed materials because of the exothermic reaction. The use of **13**-HCOOH-CH_3CN system[5] for the nitration of **6a** at room temperature led to the production of a small amount of 2-nitrofuran (5%) and large amounts of decomposed materials since a strongly acidic gas was evolved. We suppose that the present gas might consist of HNO_3 and its decomposition products generated by the reaction of **13** with HCOOH.

Next, we carried out a brief examination of the nitration of olefins. Some reagents such as HNO_3–Ac_2O,[10] N_2O_4,[11] **13**-HCOOH–CH_3CN[5] and CAN-cyclohexanone–HCOOH–CH_3CN[5] have been reported. Our method is also useful for the nitration of olefins. The treatment of olefins **10a–12a** with **13** in Ac_2O led to the nitroacetates together with small amounts of nitroolefins (entries 10–12). It is noteworthy that activated olefin **12a** readily reacts with **13** in Ac_2O at room temperature to give adduct **12b**.

In conclusion, owing to its simplicity and mildness, the present procedure provides a highly efficient method for the nitration of aromatic and olefinic compounds.

Experimental

Melting points are uncorrected. The IR spectra were recorded on a HITACHI I-3000 spectrophotometer. The ^1H NMR spectra were measured on a Hitachi R-24B spectrometer using tetramethylsilane as an internal standard. Cerium (III) ammonium nitrate tetrahydrate (**13**) was purchased from Wako Pure Chemical Industries.

> **Caution**: Reactions using HNO_3–Ac_2O must be carried out at low temperature and in appropriate proportions in order to prevent overheating or detonation.[12] Attention should also be paid for the reactions of active compounds such as pyrrole with $(NH_4)_2Ce(NO_3)_5$ in Ac_2O for overheating.

Typical procedure for the nitration of aromatic compounds with **13**: A mixture of **4a** (9.0 mmol) and $(NH_4)_2Ce(NO_3)_5$·$4H_2O$ (3.3 mmol) in Ac_2O (7.5 cm³) was stirred at room temperature for 14 h.

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.
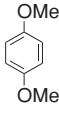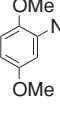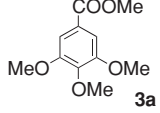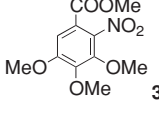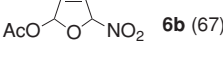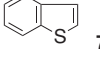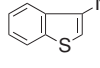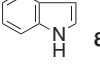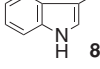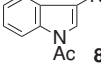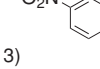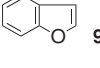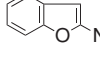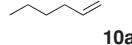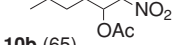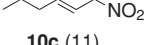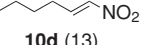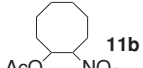
The reaction mixture was poured onto crushed ice (10 g) and extracted with EtOAc. The extracts were washed with water, dried and evaporated. The residue was chromatographed (hexane-acetone = 10 : 1) on silica gel to give **4b** (58%) and **4c** (12%).

Compounds obtained in this study were identified by comparison of their spectroscopic behaviors with authentic (**2b**,[13] **2c**,[14] **3b**,[3] **4b,c**,[2] **5b**,[15] **6b**,[9] **7b**,[16] **8b**,[17] **9b**,[18] **10d**[19] and **11d**[19]) or commercially available samples. Other analytical data are presented below. Compounds **6b**, **11b** and **12b** were obtained as an inseparable mixture of diastereomers, but the stereochemistry was unknown.

5-Nitro-2,5-dihydrofuran-2-yl acetate (**6b**):[9] Colourless oil (Found: C, 41.3; H, 4.0. $C_6H_7NO_5$ requires C, 41.6; H, 4.1%); ν_{max} (neat)/cm^{-1} 1756, 1570, 1374, 1226, 1146, 1098; δ_H (CD$_3$COCD$_3$) 2.10 (3H, s, OAc), 6.45–7.34 (4H, m, CH and C=CH).

1-Acetyl-3-nitroindole (**8c**): Yellow needles, m.p. 157–158 °C (from benzene) (Found: C, 59.0; H, 4.0. $C_{10}H_8N_2O_3$ requires C, 58.8; H, 3.9%); ν_{max} (KBr)/cm^{-1} 3140, 1740, 1588, 1552, 1504, 1480, 1384, 762; δ_H (CDCl$_3$) 2.87 (3H, s, COCH$_3$), 7.40–7.64 (2H, m, ArH), 8.17 (1H, dd, J = 7.0 and 7.0 Hz, ArH), 8.45 (1H, dd, J = 7.0 and 7.0 Hz, ArH), 8.80 (1H, s, 2-H).

Table 1   The reactions of substrates **1a–12a** with cerium (III) ammonium nitrate in Ac$_2$O

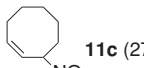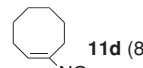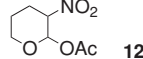| Entry	Substrate	Temp. (°C)	Time/h	Products (Yield/%)[a]
1	**1a**	25	14	**1b** (90)
2	**2a**	60	7	**2b** (54) **2c** (4) **2d** (34)
3	**3a**	60	2	**3b** (82)
4	**4a**	25	17	**4b** (58) **4c** (12)
5	**5a**	25	24	**5b** (80)
6	**6a**	25	9	**6b** (67)
7	**7a**	25	72	**7b** (80)
8	**8a**	25	24	**8b** (31) **8c** (13) **8d** (3)
9	**9a**	25	24	**9b** (61)
10	**10a**	60	12	**10b** (65) **10c** (11) **10d** (13)
11	**11a**	60	5	**11b** (65) **11c** (27) **11d** (8)
12	**12a**	25	24	**12b** (84)

[a]Isolated yields.

Table 2   The comparison of melting points of observed with those in the literature

Compound	M.p. (observed)/°C	M.p. (literature,[ref.])/°C
1b	72–73 (hexane)	71–73[21]
2d	52–53 (EtOH)	53 (EtOH)[13]
3b	67–68 (hexane)	67–68[3]
4b	43–44 (ether-hexane)	44–45 (petroleum ether)[2]
4c	75–76 (EtOH)	77 (EtOH)[2]
5b	61–63 (benzene-hexane)	65–66.5 (light petroleum)[12]
7b	80–81 (benzene)	81 (benzene)[13]
8b	208–209 (benzene)	210 (benzene)[14]
8d	138–140 (benzene-hexane)	140–141 (benzene-cyclohexane)[22]
9b	131–132 (MeOH)	134 (MeOH)[15]

1-Nitromethylpentyl acetate (**10b**): Colourless oil (Found: C, 60.9; H, 9.5. $C_8H_{15}NO_2$ requires C, 61.1; H, 9.6%); ν_{max} (neat)/cm^{-1} 2964, 2876, 1746, 1554, 1458, 1378; δ_H (CD$_3$COCD$_3$) 0.91 (3H, t, J = 7.0 Hz, CH$_3$), 1.21–1.81 (6H, m, CH$_2$), 2.01 (3H, s, OAc), 4.35–4.82 (3H, m, CH$_2$ and CH).

1-Nitro-2-hexene (**10c**): Colourless oil (Found: C, 55.5; H, 8.7. $C_6H_{11}NO_2$ requires C, 55.8; H, 8.6%); ν_{max} (neat)/cm^{-1} 2960, 2868, 1528, 1468, 1354, 968; δ_H (CD$_3$COCD$_3$) 0.92 (3H, t, J = 7.0 Hz, CH$_3$), 1.15–1.85 (2H, m, CH$_2$), 1.90–2.48 (2H, m, CH$_2$), 4.30–6.00 (3H, m, C=CH and CH$_2$).

2-Nitrocyclooctyl acetate (**11b**): Colourless oil (Found: C, 55.9; H, 8.1. $C_{10}H_{17}NO_4$ requires C, 55.8; H, 8.0%); ν_{max} (neat)/cm^{-1} 2940, 1734, 1548, 1452, 1370; δ_H (CD$_3$COCD$_3$) 1.40–2.49 (12H, m, CH$_2$), 1.97 (3H, s, OAc), 4.50–5.04 (2H, m, CH).

3-Nitrocyclooctene (**11c**):[20] Colourless oil (Found: C, 61.7; H, 8.2. $C_8H_{13}NO_2$ requires C, 61.9; H, 8.4%); ν_{max} (neat)/cm^{-1} 2936, 2860, 1544, 1468, 1374; δ_H (CD$_3$COCD$_3$) 1.30–1.90 (6H, m, CH$_2$), 1.90–2.52 (4H, m, CH$_2$), 4.61 (1H, td, J = 7.0 and 1.0 Hz, CH), 5.42–6.11 (2H, m, C=CH).

3-Nitrotetrahydropyran-2-yl acetate (**12b**): Colourless oil (Found: C, 48.7; H, 6.5. $C_7H_{11}NO_4$ requires C, 48.6; H, 6.4%); ν_{max} (neat)/cm^{-1} 2964, 1740, 1552, 1442, 1372, 1010; δ_H (CD$_3$COCD$_3$) 1.30–2.24 (7H, m, OAc and CH$_2$), 3.40–3.80 (2H, m, CH$_2$), 3.91–4.21 (1H, m, CH), 4.41–4.75 (1H, m, CH).

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